hundred microliters each of DOPE:DODAC:PEG-Cer(C_{20}) control particles was injected into one group of three female ICR mice and 200 μL of DOPE:DODAC:PEG-Cer(C_{14}) control particles was injected into three groups of three of the ICR mice. The plasma was analyzed for ^{14}C-lipid after 1, 2 and 5 hours.

FIG. **20** shows the clearance of DNA encapsulated in particles composed of DOPE:DODAC:PEG-Cer(C_{20}) ((83.5:6.5:10 mole %). The DNA and lipid are cleared much less rapidly from the circulation than when PEG-Cer(C_{14}) is used (see FIG. **21**). Nearly 50% of the lipid and DNA are present after 1 hour. A significant amount of DNA and lipid were still present after 5 hr. The amount of DNA and lipid injected was 1.8 μg and 853 μg, respectively. Control particles exhibited a clearance similar to that of the plasmid-lipid particles.

FIG. **21** shows the clearance of DNA encapsulated in particles composed of DOPE:DODAC:PEG-Cer(C_{14}) ((83.5:6.5:10 mole %). Both DNA and lipid are cleared rapidly from the circulation with only about 20% of the lipid and 10% of the DNA present in the plasma after 1 hr. The amount of DNA and lipid injected was 2.7 μg and 912 μg, respectively. Control particles exhibited a clearance similar to that of the plasmid-lipid particles.

In Vivo Transfection in Lung, Liver and Spleen

Three groups of four IRC mice were injected via tail vein with pCMV4-CAT encapsulated in lipid particles composed of DOPE:DODAC:PEG-Cer(C_{14}) (83.5:6.5:10 mole %, "A") or DOPE:DODAC:PEG-Cer(C_{20}) (83.5:6.5:10 mole %, "B"), prepared as described above. The mice were sacrificed after 2, 4 and 8 days and the lung, liver and spleen were assayed for CAT activity according to a modification of Deigh, *Anal. Biochem.* 156:251–256 (1986). The amount of plasmid injected was 2.6 μg for the particles containing PEG-Cer(C_{14}) and 1.5 μg for the particles containing PEG-Cer(C_{20}).

FIG. **22** shows the results of in vivo transfection achieved in the lung. As can be seen from this figure, treatment with formulation "A" provided excellent transfection efficiency (based on CAT activity) up to 4 days. Formulation "B", while resulting in overall lower levels of CAT activity, provided relatively constant levels of enzyme activity over 8 days.

FIG. **23** shows the results of transfection achieved in the liver. For both formulations, transfection (and CAT activity) reached a maximum at 4 days.

FIG. **24** shows the results of transfection achieved in the spleen wherein the maximum transfection was found for both formulations to occur after 2 days.

VII. Conclusion

As discussed above, in accordance with one of its aspects, the present invention provides methods for preparing serum-stable plasmid-lipid particles which are useful for the transfection of cells, both in vitro and in vivo.

All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious that certain changes and modifications may be practiced within the scope of the appended claims.

What is claimed is:

1. A nucleic acid-lipid particle for introducing a nucleic acid into a cell, said particle comprising a cationic lipid, a non-cationic lipid, and a nucleic acid, wherein said nucleic acid in said nucleic acid-lipid particle is resistant in aqueous solution to degradation by a nuclease.

2. The particle of claim **1**, wherein said particle has a diameter of from about 50 to about 150 nm.

3. The particle of claim **2**, wherein said particle has a diameter of from about 65 to about 85 nm.

4. The particle of claim **1**, wherein said cationic lipid is selected from the group consisting of DODAC, DDAB, DOTAP, DOTMA, DOSPA, DOGS, DC-Chol, and combinations thereof.

5. The particle of claim **1**, wherein said non-cationic lipid is selected from the group consisting of DOPE, POPC, EPC, and combinations thereof.

6. The particle of claim **5**, wherein said non-cationic lipid further comprises a PEG-lipid.

7. The particle of claim **6**, wherein the concentration of said PEG-lipid within said particle is from about 1% to about 15%.

8. The particle of claim **6**, wherein said PEG-lipid is PEG-ceramide.

9. The particle of claim **1**, wherein said cationic lipid comprises from about 1% to about 53% of the lipid present in said particle.

10. The particle of claim **1**, wherein said non-cationic lipid comprises from about 37% to about 89% of the lipid present in said particle.

11. The particle of claim **1**, wherein said nucleic acid is DNA.

12. The particle of claim **1**, wherein said nucleic acid is selected from the group consisting of a plasmid, an antisense oligonucleotide, and a ribozyme.

13. The particle of claim **1**, wherein a plurality of said particles is non-aggregating in solution.

14. The particle of claim **1**, wherein the nucleic acid component of said particle is substantially not degraded after incubation of said particle in serum at 37° C. for 30 minutes.

15. The particle of claim **1**, wherein more than 10% of a plurality of said particles are present in blood 24 hours after injection.

16. The particle of claim **1**, wherein transformation of cells in the lung or liver is detectable at least 4 days after injection of said particle.

17. A pharmaceutical composition comprising a nucleic acid-lipid particle of claim **1**, and a pharmaceutically acceptable carrier.

18. A method of introducing a nucleic acid into a cell, said method comprising contacting said cell with a nucleic acid-lipid particle of claim **1**.

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